

REMARKS

Claims 1, 26-27, 32-35, 40-41, 45-46, 59, 67, 80, 91-92, 94-98, 101, 103-113, 115, 120, 122-127, 131, 155-156, and 158-160 are pending in this application prior to entry of this amendment. Claims 120, 122-127, 131 (in part), and 159 of Groups III and V of the previous restriction requirement were withdrawn from consideration by the Examiner. Claims 109, 120, 122-127, 155, and 159 have been canceled. Claims 1, 91, 101, 108, and 131 have been amended to recite that R^{1a} - R^{1e} are independently H, Cl, or F; R^2 is methyl; R^3 is Cl or Br; R^4 is methoxy; and R^5 is H. Claims 59 and 101 have been amended to recite that the halogenating reagent is a chlorinating or a brominating reagent. Claims 1, 32, 46, 59, 67, 80, 91, 101, and 108 have been amended to cancel the phrase "for a time and under conditions suitable for forming a compound...". Claim 131 has been amended to delete Formulas (II) and (VI); and to delete the definitions of R^{2a} and R^{2b} as superfluous in light of the deletion of Formula (VI). Support for the amendments can be found throughout the specification and original claims, for example, in original claim 25 (R^{1a} - R^{1e} are independently H, Cl, or F; R^2 is methyl; R^3 is Cl or Br; R^4 is methoxy; and R^5 is H); in original claims 60-61 and 102 (halogenating reagent is a chlorinating or brominating reagent); in claim 131 (new claim 161); and in the Examples. No new matter has been added. After entry of this amendment, claims 1, 26-27, 32-35, 40-41, 45-46, 59, 67, 80, 91-92, 94-98, 101, 103-108, 110-113, 115, 131, 156, 158, and 160 will be pending in this application.

I. Error in Disposition of Claims

Applicants note that the second page of the Office Action incorrectly lists claims 36-39 as pending. These claims were canceled in a preliminary amendment filed on September 21, 2006. Further, the second page of the Office Action also fails to list claims 33-34 which are currently pending. Applicants respectfully request correction of the Office's records.

II. Restriction Requirement

Applicants thank the Examiner for rejoining Groups I, II, and IV of the restriction requirement. Applicants have amended the claims to cancel the withdrawn subject matter of Groups III and V.

III. Rejections under 35 U.S.C. § 112, ¶ 2

Claims 1, 26-27, 32, 35, 40-41, 45-46, 59, 67, 80, 91-92, 94-98, 101, 103-113, 115, 131, 155-156, 158, and 160 are rejected under 35 U.S.C. § 112, ¶ 2 as being allegedly indefinite with regard to the phrase “for a time and under conditions suitable for forming a compound...”. Claims 1, 32, 46, 59, 67, 80, 91, 101, and 108 have been amended to cancel this phrase, solely to advance prosecution. Applicants respectfully request that the claim rejections be withdrawn.

IV. Rejections under 35 U.S.C. § 103(a)

Claims 1, 26-27, 32, 35, 40-41, 45-46, 59, 67, 80, 91-92, 94-98, 101, 103-113, 115, 131, 155-156, 158, and 160 are rejected under 35 U.S.C. § 103(a) as being allegedly obvious over U.S. Patent No. 6,140,509 (“Behan”). With respect to claim 1, the Office alleges that Behan discloses an analogous process for preparing a compound of Formula (I) by reacting an isocyanate compound of Formula (III) or (IIa) with an amine compound of Formula (II) or (IIIa). The Office further alleges that Behan discloses analogous processes to those recited in claims 91, 101, 108, but does indicate any particular section of Behan other than the “reaction schemes”.

Applicants respectfully assert that the processes of claims 1, 91, 101, and 108 and the intermediate compounds of Formulas (IV) and (V) in claim 131 are non-obvious over the processes and intermediate compounds in Behan. In interpreting the Supreme Court’s decision in *KSR Int’l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1739, 82 U.S.P.Q.2d 1385 (2007), the Federal Circuit held that a *prima facie* finding of obviousness for a claim involving a chemical compound depends on three factors:

First, KSR assumes a starting reference point or points in the art, prior to the time of invention, from which a skilled artisan might identify a problem and pursue potential solutions. Second, KSR presupposes that the record up to the time of

invention would give some reasons, available within the knowledge of one of skill in the art, to make particular modifications to achieve the claimed compound... Third, the Supreme Court's analysis in KSR presumes that the record before the time of invention would supply some reasons for narrowing the prior art universe to a "finite number of identified, predictable solutions," 127 S. Ct. at 1742. In *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc.*, 520 F.3d 1358, 1364 [86 USPQ2d 1196] (Fed. Cir. 2008), this court further explained that this "easily traversed, small and finite number of alternatives ... might support an inference of obviousness." To the extent an art is unpredictable, as the chemical arts often are, KSR's focus on these "identified, predictable solutions" may present a difficult hurdle because potential solutions are less likely to be genuinely predictable.

Eisai Co. Ltd. v. Dr. Reddy's Laboratories Ltd., 87 U.S.P.Q.2d 1452, 1456-57 (Fed. Cir. 2008) (further noting that "post-KSR, a *prima facie* case of obviousness for a chemical compound still, in general, begins with the reasoned identification of a lead compound"). Accordingly, in establishing a *prima facie* case of obviousness for a chemical compound (or a process of producing a particular chemical compound), the Office bears the burden of showing: (1) a reasoned identification of a lead compound; and (2) some reason that would have led a chemist to modify the lead compound in a particular manner. The Office has entirely ignored the first factor and failed to provide any evidence to address the second factor, as detailed below.

A. No reasoned identification of a lead compound

The Office has not identified a lead compound in Behan, which one of ordinary skill in the art could modify to arrive at compounds of Formula (I), (IV) or (V). Instead, the Office merely generally indicates various schemes for making different urea compounds in Behan. The reasoned identification in *Takeda* is not some optional test that can be ignored in establishing a *prima facie* case of obviousness. See *Eisai*, 87 U.S.P.Q.2d at 1457 (finding that "a *prima facie* case of obviousness for a chemical compound still...begins with the reasoned identification of a lead compound", which only be established by supported assertions). Further, a reasoned identification of a lead compound requires more than just structural similarity between the claimed and prior art compounds. *Takeda*, 83 U.S.P.Q.2d 1169, 1175 (Fed. Cir. 2007) (finding

that the most structurally similar prior art compound was not a "lead compound" based, in part, on test results showing that it was "not one of the three most favorable compounds"; *see also*, *Eisal* at 1456 (finding a lead compound based on its higher activity and other desirable properties, rather reliance on structural similarity). Hence, by failing to provide a reasoned identification of a lead compound in Behan, the Office has failed to establish a *prima facie* case of obviousness.

B. No reason to modify the hypothetical lead compound in a particular manner

Even assuming *arguendo* that the Office had presented a reasoned identification of a lead compound, the Office has provided no evidence to support making the specific molecular modifications necessary to arrive at the compounds of Formula (I), (II), (IV), or (V), such as the modifications in the process claims herein. Instead, the Office relies solely on alleged structural similarity in contravention of *Takeda*. As acknowledged by the Office, the compounds of Formulas (I), (II), (IV), and (V) differ from the Behan compounds by having a non-H substituent at the R⁴ position.¹ By contrast, the phenyl ring in each Behan compounds is unsubstituted at the R⁴ position. The Office alleges that a simple substituent like methyl is a homologue of the unsubstituted compound, but provides no reasons for making the specific molecular modification other than this reliance on alleged structural similarity.

In order to further prosecution, Applicants have amended the claims to recite that R⁴ is methoxy, R³ is Cl or Br, R² is methyl, R^{1a}-R^{1e} are independently H, Cl, or F, and R⁵ is H, further differentiating the claimed compounds from the Behan compounds. Applicants respectfully

¹ Applicants respectfully point out that Behan et al. teaches the synthesis of methylpyrazole derivatives from a starting material represented by intermediate 1, below. To that end, the Behan inventors report one source of intermediate 1 as Maybridge Chemical Co. (Catalog No. KM01978, CAS No. 175201-77-01). Vendor literature indicated that the information in Behan about intermediate 1 was correct. After Behan et al. filed their application, individuals at Arena Pharmaceuticals, the owner of both Behan et al. and the instant application, determined that the material marketed by Maybridge actually had the structure corresponding to intermediate 2. As a result, the structures disclosed in Behan, such as Compound No. 116081 could not be synthesized using the intermediate originally obtained by Arena from Maybridge Catalog No. KM01978. Arena subsequently filed a second application (WO 2002/076464) depicting a compound (also labeled Compound No. 116081) that was made using intermediate 2 rather than intermediate 1, thus resulting in a regioisomer of the structure originally reported in Behan with the methyl group on the other nitrogen of the pyrazole ring.



assert that Behan provides no reason for modifying R⁴ from a hydrogen atom to a methoxy group. Indeed, the broadest generic disclosure in Behan shows that the position corresponding to R⁴ is always hydrogen (see e.g., Behan at column 22, line 8, through column 25, line 26). By fixing R⁴ as hydrogen throughout the disclosure, Behan itself suggests that a lack of substitution at R⁴ is critical for activity. Accordingly, one of ordinary skill in the art would simply not have a motivation for making the specific modification of replacing a hydrogen atom with a methoxy group at the R⁴ position. Accordingly, the Office has not carried its burden to show a reason for making the particular structural modifications necessary to arrive at the claimed compounds.

Further, the Office has not demonstrated that any of the synthetic steps for making compounds of Formulas (II), (IV), and (V) in claims 91, 101, and 108, respectively, are disclosed in Behan. Applicants have been unable to locate any portion of Behan which discloses the synthetic steps in claims 91, 101, and 108. Hence, in addition to failing to show a motivation for making compounds of Formula (II), (IV), or (V) via the claimed processes, the Office has also not shown that Behan teaches or suggests the synthetic methodology in claims 91, 101, or 108.

For at least these reasons, Applicants respectfully assert that a *prima facie* case of obviousness has not been established and request that the rejections be withdrawn.

V. Obviousness-type Double Patenting

Claims 1, 26-27, 32, 35, 40-41, 45-46, 59, 67, 80, 91-92, 94-98, 101, 103-113, 115, 131, 155-156, 158, and 160 are provisionally rejected over claims 1-56 of copending application ser. no. 11/883,043 ("the '043 application") under the doctrine of obviousness-type double patenting (OTDP). The present application, however, was filed on September 21, 2006, before the '043 application. As will be appreciated, when a "provisional nonstatutory obviousness-type double patenting...rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer". M.P.E.P. § 804. Applicants respectfully assert that the current

amendments and remarks overcome the rejections of record and request that the OTDP rejection be withdrawn.

VI. Information Disclosure Statement

Applicants will be filing a supplemental information disclosure statement within the next few days for the Examiner's consideration.

VII. Conclusion

Applicants respectfully assert that the claims are in condition for allowance and an indication of the same is respectfully requested. The Examiner is encouraged to contact Applicants' representative at the number below if there are any questions regarding the above-captioned application.

The Commissioner is hereby authorized to debit any fee due or credit any overpayment to Deposit Account No. 06-1050. Further, if not accompanied by an independent petition, this paper constitutes a Petition for an Extension of Time for an amount of time sufficient to extend the deadline and authorizes the Commissioner to debit the petition fee and any other fees or credits to Deposit Account No. 06-1050 referencing Attorney Docket No. 20750-0050US1.

Respectfully submitted,



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